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Monitoring During Cryosurgery of Bone Tumors

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Background: Cryosurgery is used in orthopaedic oncology as adjuvant treatment after intralesional excision of bone tumors to induce cell death at and beyond the surgical margin. Monitoring freeze/thaw cycles during cryosurgery is beneficial in controlling a cryosurgical procedure and in preventing an unwarranted local extent of the freeze.
Method: We conducted a study of 15 cryosurgical procedures with the use of a protocolized temperature measuring system with peroperative graphic visualization.
Results: Using a liquid nitrogen spray, intralesional temperatures of −150°C were achieved, which are, according to the literature, associated with cell death. Extralesional temperature measurements showed no subzero temperatures of surrounding important tissues.
Conclusions: Temperature recordings in and outside the lesion during cryosurgery in orthopaedic oncology are of importance to monitor the freeze/thaw cycles and are helpful in facilitating an effective cryosurgical procedure and in controlling the extent *of* the freeze, avoiding local complications. *J. Surg. Oncol. 1997;65:40–45.* © 1997 Wiley-Liss, Inc.

KEY WORDS: cryotherapy; skeletal neoplasm; complications; recording

INTRODUCTION

Cryosurgery utilizing liquid nitrogen is practiced in orthopaedic oncology for the treatment of primary benign and malignant bone tumors as well as for secondary metastases to bone. In benign and low grade malignant stage IA skeletal tumors [1], it is used as an adjuvant treatment to intralesional resection (curettage) to extend the surgical margin of excision [2–10]. By this method the procedure can be considered to be marginal according to oncologic principles [1]. The advantage of this kind of treatment, as compared to local resection, is that as much as possible of the supportive function of bone is preserved and that reconstructive surgery can be limited. In high grade sarcomas, cryosurgery has been used as the primary treatment with variable results [10,11]. Cryosurgery used in the treatment of bony metastases has to be considered as palliative and in this respect helpful in local control of the malignancy [12,13].

Since the introduction of cryosurgery in medicine, monitoring modalities have been developed to visualize the local process for the following reasons:

a. To ensure that lethal temperatures for tumor cell death are reached. The temperature of frozen tissue cannot be determined by its visual appearance alone, since frosted tissue looks the same at any freezing temperature [14,15].
b. An accurate measurement of the depth and lateral spread of the freeze is necessary, not only for obtaining adequate margins, but also to avoid an unwarranted extension of the freezing inducing potential morbidity [15].
c. Local temperature measurement enables a more pre-

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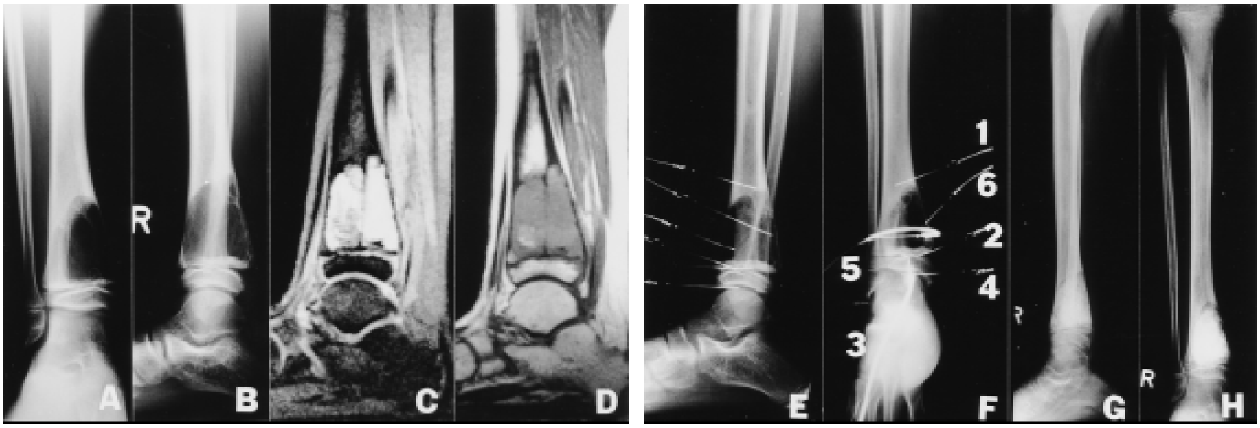


Fig. 1. Routine radiographs of an 11-yr.-old boy with aneurysmal bone cyst in the distal tibia, very close to the growthplate (**A,B**). Magnetic resonance imaging, T2 (**C**) and T1 (**D**), showing erosion of the cortex and a fairly homogeneous intensity of the contents of the cyst consistent with fluid. Intraoperative radiographs showing localization of the temperature couples. Number 2 and 3 are situated in the growthplate, number 4 is intra-articular (**E,F**). The intralesional temperature couple, number 7 was added later. Numbers correspond with those in Figure 3A. After curettage and cryosurgery, the cyst is filled with a homologous bonegraft (**G,H**).

cise determination of the ending of the thawing phase. Complete spontaneous warming up of the frozen tissue before the next freeze/thaw cycle is started is important to induce a maximum lethal effect on tumor cells [16].

d. Monitoring, and preferably recording of the cryosurgical procedure, enables the physician to evaluate the procedure itself and interpret follow-up results with respect to the procedure. Adjustments in technique can be developed and introduced. Scientific research on recorded data will ultimately improve the quality of cryosurgery.
e. Recording of the whole freezing procedure provides written evidence, which may be of medicolegal importance.

Next to local monitoring, systemic monitoring seems to be of importance, because whenever a gas is introduced into a body cavity, there is always the hazard of intravascular introduction of gas bubbles. Gas emboli in the vascular circulation can cause serious hemodynamic complications and has been associated with potentially lethal circulatory and pulmonary complications [17–19]. Cryosurgery of bone tumors is in this perspective no exception and has been associated with (lethal) complications in the past [20,21].

This report describes the technical details and results of local monitoring with thermocouples during cryosurgery of bone tumors (Figs. 1A–D, 2A–D).

MATERIALS AND METHODS

For the local monitoring of cryosurgery of bone tumors, we developed a multifocal temperature measuring system utilizing up to nine thermocouples. The thermocouples consist of a copper/copper-nickel alloy and are mounted in the tip of a 50-mm-long and 0.8-mm diameter injection-like needle (Ellab A/S; Roedovre, Denmark). Their accuracy is better than 0.1°C with a response time of 0.3 s. Temperature data acquisition was done using a digital multimeter (Digital multimeter 2000, Keithley Instruments, Cleveland, OH) equipped with a thermocouple scanner card (2001-TCSCAN, Keithley Instruments). Graphical real-time visualization of the course of the temperatures is accomplished by connecting the multimeter to a personal computer running appropriate ‘‘homemade’’ software. Next to performing real-time display, this program stores all temperature data for later analysis.

After exposure of the tumor, bony fenestration is performed followed by intralesional resection (curettage) of the tumor. Thermocouples are placed according to a fixed protocol: two to monitor the axial intramedullary spread of the freeze, respectively, proximal and distal of the lesion, and two or more extra cortical, around the lesion to monitor the lateral spread of the freeze. One thermocouple is situated in the lesion itself and reflects the intralesional surface temperature. Additional thermocouples can be used adjacent to structures that should not be damaged, such as neurovascular bundles and growthplates, or in joints to prevent damage of the articular cartilage. Intraoperative radiographs are used to document the location of the thermocouples more precisely (Figs. 1E, F, 2E, F).

Three cycles of cryosurgery are performed using a machine producing a liquid nitrogen spray (Erbokryo NL, ERBE, Nieuwegein, The Netherlands). The duration of each freeze is based on the temperature readings and visual observation. Warming up is done by spontaneous thawing. Reconstruction of the bony defect is carried out

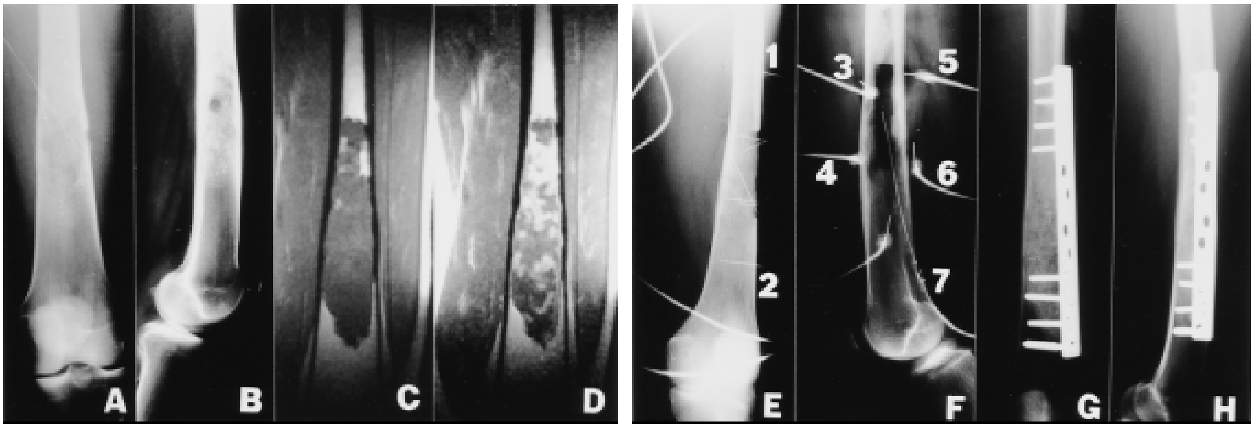


Fig. 2. Postbiopsy routine radiographs of a 29-yr.-old female with chondrosarcoma, grade 1 of diaphysis of the femur (**A,B**). Magnetic resonance imaging, T1 (**C**) and T2 (**D**) weighed showing erosion of cortex and an inhomogeneous signal intensity consistent with enchondroma or low-grade chondrosarcoma. Intraoperative radiographs showing localization of the temperature couples. Number 7 is situated in the curetted lesion. Numbers correspond with those in Figure 3B (**E,F**). After curettage and cryosurgery, the cyst is filled with homologous bonegraft (**G,H**).

with an autologous and/or homologous bonegraft (Figs. 1G,H, 2G,H).

The protocolized temperature measurement system was used in 15 patients (5 females, 10 males) with a mean age of 31.7 yrs (range 11–64), all having active or aggressive benign lesions [1], which are specified in Table I.

RESULTS

Every patient had almost similar temperature recordings during their three freeze-thaw cycles. Two typical examples are shown in Figure 3A,B. In all cases the intralesional recording, which reflects the surface temperature of the bony cavity, reaches −50°C in a mean time of 10.6 s (range: 8–15s) after the spraying with liquid nitrogen is started. A temperature of −150°C and below was easily achieved in all cases, with the exception of two giant cell tumors of the distal radius. Continuous spraying for 15–20 s resulted in an intralesional temperature of −50°C or below during a mean of 39.3 s (range: 22–88s). Spontaneous thawing between −50° and 0°C took on the average 152.6 s (range: 30–420s). In this period the increasing temperature frequently entered a subzero plateaux phase varying in time from 20s to 250 s. Thawing from 0 to 20°C required in general 290 s (range: 90–900s). In Table II these monitoring readings are specified for, respectively, the first, second, and third cycles. Thermocouples monitoring the axial and lateral spread of the freeze showed a delayed temperature decrease, but it almost never dropped below 0°C. The temperature recorded by the extracortical thermocouples, which are only separated from the freeze by the thickness of the cortex, sometimes declined just below 0°. In general, the whole area around the frozen lesion cooled down, lengthening the time needed for thawing to 20°C after every freeze (Figure 3).

DISCUSSION

The common practice of monitoring a cryosurgical procedure guided by the physician's clinical judgment and experience is found particularly in freezing *soft* tissue lesions. The progress of the treatment can be followed by observation and palpation, and the depth of freezing can be estimated by observing the lateral spread of freezing in the target tissue [15,22]. Although clinical judgment of freezing extent is reasonably accurate, it is probably not enough to perform a controlled cryosurgical procedure when tissues with different thermal characteristics are involved. In orthopaedic oncology, these are cortical bone, intramedullary spongiosa, and soft tissues, mainly muscle. To supplement clinical judgment during cryosurgery, a range of monitoring devices and techniques has been developed, most to address monitoring needs for specific applications of cryosurgery. Measurement modalities are thermography [23], which involves very expensive equipment and provides only surface freezing evaluation [15], ultrasound [24,25], which is not suitable for bony tissue, and tissue impedance and resistance measurements [26–28], which causes concern about accuracy [15]. Computerized tomography [29] and magnetic resonance [30–32] are capable of visualizing frozen tissue, but their high cost and the logistics involved make them unsuitable for the orthopaedic setting. In this perspective we developed our system using temperature couples.

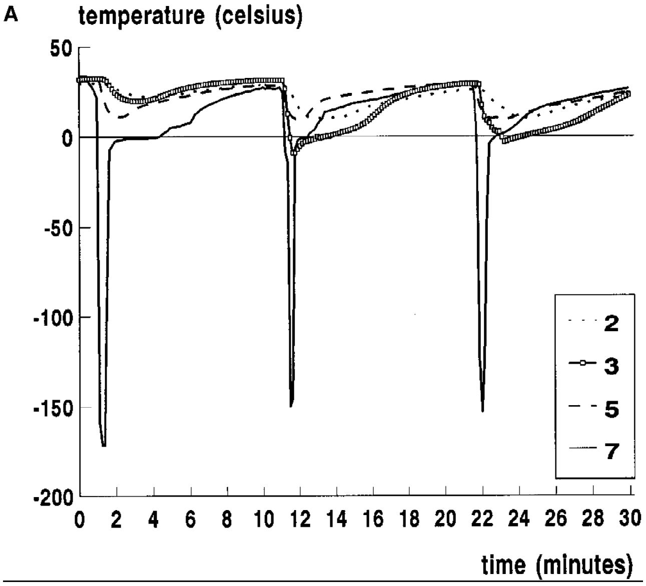
Thermocouples were first used to monitor cryosurgery of skin lesions. Their importance was recognized early in cryosurgical practice, particularly in establishing lethal temperatures [33].

Using the temperature measuring system with real-time graphical visualization, we showed that with this freezing technique, intralesional temperatures of −150°C are achieved within seconds (freezing-rate > 10°C.s^{-1}).

TABLE I. Anatomical Distribution and Diagnosis of 15 Skeletal Tumors Treated With Curettage, Cryosurgery, and Bonegrafting

Location/diagnosis	Humerus	Pelvis	Femur	Tibia	Radius	Total
GCT[a]	1		1		2	4
ABC[b]		1		1		2
SBC[c]	3			1		4
Chondroblastoma	1		1			2
Enchondroma			3			3
Total	5	1	5	2	2	15

[a]Giant cell tumor.
[b]Aneurysmal bone cyst.
[c]Simple bone cyst.



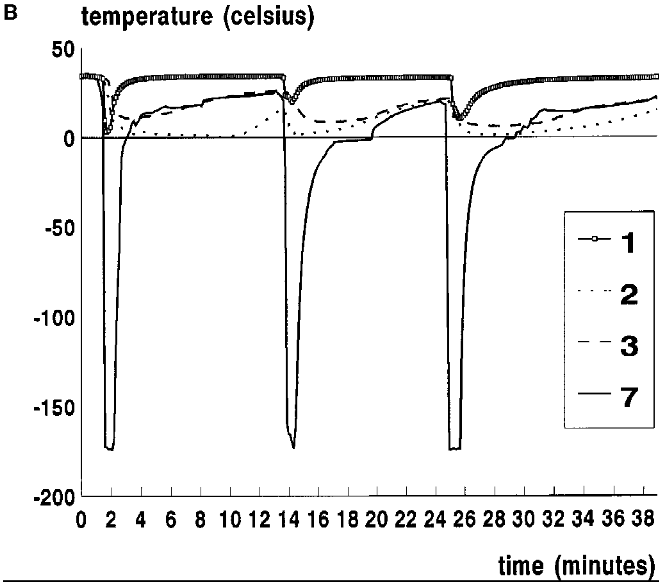


Fig. 3. **A.** Temperature recordings of patient in Figure 1; numbers correspond with those in Figure 1(E,F). The temperature measured by the thermocouples 1,4, and 6 were at all times above 25°C. For reasons of clarity of the graph, they are not shown. **B.** Temperature recordings of patient in Figure 2; numbers correspond with those in Figure 2E,F. The temperature measured by the thermocouples 4,5, and 6 were at all times above 10°C. For reasons of clarity of the graph, they are not shown.

TABLE II. Temperature Monitoring of 15 Cryosurgical Procedures Included in This Study*

Temperature phase	37°C → −50°C			−50°C and lower			−50°C → 0°C			0°C → 20°C		
Cycle	1	2	3	1	2	3	1	2	3	1	2	3
Mean time (s) per cycle	9.5	11.5	10.7	40.1	36.0	41.7	136.8	165.0	156.0	221.7	294.3	354.0
Mean time (s) 3 cycles		10.6			39.3			152.6			290.0	

*Mean time of temperature phase per cycle (1,2, or 3) and of all 3 cycles.
(s) = seconds.

Furthermore, the maintenance of a temperature of −50°C for 40 s, the apparent holding of this low temperature and the tissue in frozen state for 3 min, followed by spontaneous slow thawing and repetition of freeze/thaw cycles are all of importance to maximize tissue destruction [16,34].

Using extralesional thermocouples, we were able to show that important structures were not subjected to subzero, potentially damaging temperatures. Furthermore, extralesional thermocouples enable the surgeon to optimize the duration and lateral spread of the freeze. Extremely high freezing rates by spraying liquid nitrogen are achieved. These rates are associated with intracellular formation of ice crystals, inducing mechanical damage to the cell and thus cell death [34–38].

After spraying has been stopped and thawing is al-

lowed, the extralesional thermocouples show a further lowering of temperature, representing the retraction of tissue heat, which is used for the thawing of the more central parts of the frozen lesion. The nonlinear increase of the temperature in frozen tissue and its subzero plateau phase is explained by additional energy needed for the transition of ice into water, which halts the temperature increase temporarily.

Figure 3 shows an almost identical pattern of the freeze/thaw cycles, indicating cryosurgery utilizing a spray is a reproducible method.

The accuracy of the thermocouple readings is important as the effectiveness of treatment partially depends on it. Proper calibration and reliable hardware (good quality of thermocouple, wiring, electrical connections, and display devices) are imperative. Even more critical is the correct placement of the thermocouple itself: a 1 mm variation in the thermocouple positioning can represent a 10–15°C temperature difference [39].

In addition to routine systemic monitoring of the patient, end-tidal gas analysis is performed using a mass spectrometer measuring inspired and end-tidal O_2, CO_2, N_2O, N_2 tensions and anesthetic vapor concentration. Using real-time recording of the gas analysis breath by breath makes detection of any exhaled N_2 possible, which is associated with venous nitrogen gas embolism. In this way, we hope to take appropriate action in time to prevent serious hemodynamic complications. Because we had cardiopulmonary complications in two patients, as reported earlier [21], we started to monitor our patients with peroperative transesophageal ultrasound of the heart. Using this method in five cases, we did not detect any venous gas embolisms during our cryosurgical procedures.

We conclude that temperature recordings in and outside the lesion during cryosurgery in orthopaedic oncology are of importance to monitor the freeze/thaw cycles and are very helpful in facilitating an effective, reproducible cryosurgical procedure and in controlling the extent of the freeze avoiding local complications. Systemic monitoring is of paramount significance for the safety of the patient.

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